TABLE II.
Blood Pressure Readings and Blood Volume Determinations Following the Subcutaneous Administration of Paredrine Hydrobromide. Patients B.C. and J.M. received 30 mg and H.C. received 40 mg.

		Before drug at		After the drug at		
		30 min	15 min	15 min	30 min	90 min
B.C.	Blood pressure	118/80	122/80	164/88	172/100	110/74
	Total blood volume, cc	5000	5000	4975	5000	5041
J.M.	Blood pressure	120/70	120/70	168/86	194/112	130/72
	Total blood volume, cc	5855	5840	5770	5855	5870
H.C.	Blood pressure	118/72	120/70	210/110	208/110	150/80
	Total blood volume, cc	5206	5200	Specimen clotted	5265	5200

Paredrine subcutaneously.

nificant deviation in the blood volume. There was also no significant change in the hematocrit readings following the administration of the drug.

Conclusion. The administration of paredrine in doses sufficient to produce a definite and prolonged rise in blood pressure has no influence on the specific gravity of the blood and blood volume in normal individuals.

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Relative Ineffectiveness of Arsenocholine as a Methylating Agent in the Chick.

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Arsenocholine is an effective substitute for choline as a growth-promoting and antiperotic factor for the turkey and the chick.[1] In the rat, arsenocholine may assume several of the functions of choline, such as a lipotropic activity, but fails to exhibit appreciable methylating ability. The literature on the metabolism of arsenocholine in the rat has been concisely reviewed.[2] In seeking further explanation of the mechanism of growth-promoting and antiperotic effects of arsenocholine in the fowl it seemed of interest to determine whether this analogue of choline could exhibit a methylating action in such species. Since it was known that choline is capable of methylating homocysteine in the chick,[3] studies were made of the comparative activity of arsenocholine in this respect.

White Leghorn chicks were placed at hatching time on a low-choline diet[4] and maintained on this diet for 14 days in order to deplete them of choline. At 10 days of age they were carefully selected for uniform weight and vigor and divided into groups of 4 each. The individual growth rates were measured for 4 more days. All groups maintained uniform and comparable rates of growth during the latter period. They were then given the experimental diets for 8 days. A few chicks not selected for the experimental groups were kept on the low-choline diet.

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1 Jukes, T. H., *J. Nutrition*, 1940, **20**, 445; Jukes, T. H., and Welch, A. D., *J. Biol. Chem.*, in press.

2 Welch, A. D., and Landau, R. L., *J. Biol. Chem.*, 1942, **144**, 581.

3 Klose, A. A., and Almquist, H. J., *J. Biol. Chem.*, 1941, **138**, 467.

4 Jukes, T. H., *J. Nutrition*, 1941, **22**, 315.

TABLE I.

Effects of Choline and Arsenocholine on the Utilization of Homocystine for Growth of the Chick.

Pen	Diet	Supplement	Level, %	Avg % gain per day*
1	Basal arachin diet	Choline chloride	.50	1.7
2	" " "	dl-homocystine	.75	3.2
3	" " "	dl-homocystine Arsenocholine chloride	.75 .50	3.5
4	" " "	dl-homocystine Choline chloride	.75 .05	3.3
5	" " "	dl-homocystine Arsenocholine chloride Choline chloride	.75 .50 .50	5.6
6	" " "	dl-methionine Choline chloride	.60 .50	6.8
7	Low-choline diet	Choline chloride l-cystine	.20 .25	6.5
8	Practical rearing diet	None	—	6.9

*Gain in weight per day divided by mean weight for the test period and multiplied by 100.

These chicks developed a high incidence of perosis due to choline deficiency.

The basal arachin diet contained per 100 parts, calcium gluconate, 8; tricalcium phosphate, 2; dipotassium phosphate, 0.5; potassium chloride, 0.3; sodium chloride, 1; manganese sulphate monohydrate, 0.03; sodium silicate, 0.2; potassium iodide, 0.01; ferric oxide, 0.02; copper sulphate, 0.005; zinc sulphate, 0.005; magnesium sulphate, 0.3; Cellu-flour (cellulose), 5; 2-methyl-1,4-naphthohydroquinone-diphosphoric acid ester (sodium salt), 0.001; biotin concentrate (SMACO No. 1000), 0.05; yeast extract (1:4), 1; thiamin, 0.001; riboflavin, 0.001; pyridoxine, 0.001; nicotinic acid, 0.005; calcium pantothenate (dl), 0.006; cod liver oil (U. S. P.), 1; cholic acid, 0.05; deoxycholic acid, 0.1; vitamin E. distillate, 0.025; Wesson oil, 2.5; gelatin, 7; arachin, 23; d-lysine, 0.1; dl-threonine, 0.2; l-tryptophane, 0.3; l-cystine, 0.2; dl-valine, 0.5; l-tyrosine, 0.2; and Cerelose (glucose) to complete 100 parts.

The sample of gelatin used contained less than 0.1% methionine. The arachin may have contained up to 0.67% methionine and 1.51% cystine.[5] The basal arachin diet could not have contained appreciably more than 0.16% methionine and 0.55% cystine. Supplements to this diet and the results obtained are given in the table. The extent of these studies was necessarily limited by the amounts of arsenocholine and homocystine available.

Chicks fed the arachin diet supplemented with methionine and choline (pen 6) were able to grow at a rate equivalent to that of chicks fed the low-choline diet plus choline (pen 7) or the practical rearing diet (pen 8). This rate of gain, approximately 7% per day, is normal for the strain of chicks and the age period involved.

Addition of choline to the arachin diet led to only a very low rate of gain (pen 1). Addition of homocystine resulted in a somewhat greater rate of gain (pen 2), although less than one-half the normal, indicating that the chicks were able to utilize the homocystine to some extent in spite of the attempted depletion in choline and the absence of a choline supplement in the diet. The presence of ample quantities of cystine in the basal diet would seem to indicate that the small growth-promoting effect of the homocystine did not involve its conversion to cystine. It is more probable that some of the homocystine was methylated.

An essentially complete utilization of homocystine in the chick requires a choline intake

[5] Brown, W. L., *J. Biol. Chem.*, 1942, **142**, 299.

which is several times the minimum requirement for growth, perhaps as much as 0.5% of the diet.[3] It was felt, therefore, that any methylating power of arsenocholine would not be observed at dietary levels lower than 0.5%. The results obtained with the combination of homocystine and arsenocholine (pen 3) did not indicate that the utilization of homocystine was appreciably increased. A minimum addition of choline (pen 4) also did not result in an appreciable increase in the utilization of homocystine. However, an addition of 0.5% choline chloride to the combination of 0.5% arsenocholine chloride and homocystine did effect a very appreciable increase in rate of gain (pen 5).

This latter result showed that a sufficient level of choline was capable of increasing the rate of gain in the presence of arsenocholine which, in itself, was comparatively ineffective. The rate of gain, 5.5%, was somewhat short of the optimal rate, which may suggest a mildly toxic action of arsenocholine. Thus, in the case of Group 3, the possibility exists that a slight methylating capacity of arsenocholine may have been almost exactly compensated for by a mild toxic action. It was also observed, however, that chicks reared from date of hatching to 14 days on the low-choline diet plus 0.5% of arsenocholine chloride made gains that were approximately normal, hence it does not seem that the arsenocholine could have been seriously detrimental to growth. Chicks fed arsenocholine possessed a strong odor of garlic, probably due to the exhalation of trimethylarsine[2, 3]

Summary. Arsenocholine as compared to choline is relatively ineffective as a methylating agent for homocysteine in the chick.

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In Vitro Effect of Urea-Sulfathiazole Combination on Sulfathiazole-resistant Staphylococci.*

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Several investigators have reported that under certain conditions, *Diplococcus pneumoniae, Brucella, Streptococcus, Staphylococcus, Neisseria gonorrheae, Escherichia coli,*[1-6] and possibly other organisms, develop resistance to sulfonamides ("sulfonamide-fastness"). It has been suggested that the sulfonamide-fastness is due to the production

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1 Schmidt, L. H., Sesler, C., and Dettwiler, H. A., *J. Pharmacol. and Exp. Therap.*, 1942, **74**, 175.

2 Green, H. N., *Brit. J. Exp. Path.*, 1940, **21**, 38.

3 Neter, E., *Am. J. Surg.*, 1942, **58**, 69.

4 Vivino, J. J., and Spink, W. W., PROC. SOC. EXP. BIOL. AND MED., 1942, **50**, 336.

5 Stokinger, H. E., Charles, R. C., and Carpenter, C. M., *J. Bact.*, 1942, **44**, 216.

6 Schmelkes, F. C., and Wyss, O., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 263.